IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Myriam GOLEMBO et al.	Confirmation No.: 3940
Application No.: 10/664,605	Patent No.: 7,276,481 B2
Filing Date: September 15, 2003	Patent Date: October 2, 2007
For: METHOD AND COMPOSITION FOR TREATMENT OF SKELETAL DYSPLASIAS	Attorney Docket No.: 81408-4300

REQUEST FOR CERTIFICATE OF CORRECTION UNDER 37 C.F.R. § 1.323

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Patentees hereby respectfully request the issuance of a Certificate of Correction in connection with the above-identified patent. The corrections are listed on the attached Form PTO-1050. The corrections requested are as follows:

Title Page:

Before Item (30), please insert the following:

-- (60) Provisional application No. 60/276,939, filed Mar. 20, 2001. --

Support for this change appears on the signed Declaration filed on March 10, 2004 in response to the Notice to File Missing Parts.

Column 51:

Line 9 (claim 6, line 6), change "(1GF-1)" to -- (IGF-1) --. Support for this change appears in application claim 40.

Line 17 (claim 9, line 2), before "in vitro", change "hone" to -- bone --. Support for this change appears in application claim 67.

Line 36 (claim 15, line 3), after "protein fusion", delete the second occurrence of "protein". This change is requested merely to correct a typographical error.

Line 39 (claim 15, line 6), change "(1GF-1)" to -- (IGF-1) --. Support for this change appears in application claim 77.

Column 52:

Line 5 (claim 20, line 1), before "bone" insert -- a --. Support for this change appears in application claim 82.

Line 30 (claim 27, line 1), after "claim", change "**20**" to -- **26** --. Support for this change appears in application claim 93.

Line 37 (claim 28, line 6), change "(1GF-1)" to -- (IGF-1) --. Support for this change appears in application claim 94.

The requested changes are to correct errors of a clerical or typographical nature and do not involve changes that would constitute new matter or require reexamination.

A fee of $100 is believed to be due for this request. Please charge the required fees to Winston & Strawn LLP Deposit Account No. 50-1814. Please issue a Certificate of Correction in due course.

Respectfully submitted,

10/17/07
Date

Allan A. Fanucci, Reg. No. 30,256

WINSTON & STRAWN LLP
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212-294-3311

UNITED STATES PATENT AND TRADEMARK OFFICE

CERTIFICATE OF CORRECTION

PATENT NO. : 7,276,481 B2
APPLICATION NO. : 10/664,605
DATED: : October 2, 2007
INVENTOR(S) : Golembo et al.

It is certified that an error appears or errors appear in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Title Page:
Before Item (30), please insert the following:
-- (60) Provisional application No. 60/276,939, filed Mar. 20, 2001. --

Column 51:
Line 9 (claim 6, line 6), change "(1GF-1)" to -- (IGF-1) --.
Line 17 (claim 9, line 2), before "in vitro", change "hone" to -- bone --.
Line 36 (claim 15, line 3), after "protein fusion", delete the second occurrence of "protein".
Line 39 (claim 15, line 6), change "(1GF-1)" to -- (IGF-1) --.

Column 52:
Line 5 (claim 20, line 1), before "bone" insert -- a --.
Line 30 (claim 27, line 1), after "claim", change "**20**" to -- **26** --.
Line 37 (claim 28, line 6), change "(1GF-1)" to -- (IGF-1) --.

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US007276481B2

(12) United States Patent
Golembo et al.

(10) Patent No.: US 7,276,481 B2
(45) Date of Patent: Oct. 2, 2007

(54) **METHOD AND COMPOSITION FOR TREATMENT OF SKELETAL DYSPLASIAS**

(75) Inventors: **Myriam Golembo**, Moshav Netayim (IL); **Avner Yayon**, Moshav Sitria (IL)

(73) Assignee: **ProChon Biotech Ltd.**, Ness-Ziona (IL)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 311 days.

(21) Appl. No.: **10/664,605**

(22) Filed: **Sep. 15, 2003**

(65) **Prior Publication Data**

US 2004/0138134 A1 Jul. 15, 2004

Related U.S. Application Data

(63) Continuation of application No. PCT/IL02/00229, filed on Mar. 20, 2002.

(60) Provisional application No. 60/276,939, filed Mar. 20, 2001

(30) **Foreign Application Priority Data**

Mar. 20, 2001 (IL) 00142118

(51) **Int. Cl.**
A61K 38/00 (2006.01)

(52) **U.S. Cl.** **514/13**; 514/2; 435/1.1

(58) **Field of Classification Search** ..... None
See application file for complete search history.

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(57) **ABSTRACT**

The present invention discloses pharmaceutical compositions for the treatment of skeletal dysplasias, comprising as an active ingredient at least one natriuretic peptide. Unexpectedly, it has been shown that the natriuretic factors may be effective for bone elongation in situations of abnormal bone growth especially for achondroplasia. The effects of the natriuretic peptide may be further enhanced by prolonging its residence time or action at the target site.

30 Claims, 5 Drawing Sheets

5. The pharmaceutical composition according to claim 1 further comprising an inhibitor of fibroblast growth factor receptor 3 tyrosine kinase.

6. The pharmaceutical composition according to claim 1 wherein the natriuretic peptide is fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein; wherein the carrier protein is selected from the group consisting of growth hormone (GH), insulin like growth factor-1 (1GF-1) and thyroid hormone (TH).

7. The pharmaceutical composition according to claim 6 wherein the carrier protein comprises growth hormone.

8. The pharmaceutical composition according to claim 6 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

9. A method for increasing the size of a bone growth plate in a bone comprising treating the bone in vitro with an effective amount of at least one natriuretic peptide in a pharmaceutical composition according to claim 1.

10. The method according to claim 9 further comprising inhibiting the natriuretic peptide clearance receptor.

11. The method according to claim 9 further comprising an inhibitor of the neutral endopeptidase 24.11.

12. The method according to claim 11 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

13. The method according to claim 12 wherein the step of administering an inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.

14. The method according to claim 9 further comprising an inhibitor of fibroblast growth factor receptor 3 tyrosine kinase.

15. The method according to claim 9 wherein said at least one natriuretic peptide is fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein ~~protein~~ wherein the carrier protein is selected from the group consisting of growth hormone (GH), insulin like growth factor-1 (1GF-1) and thyroid hormone (TH).

16. The method according to claim 15 wherein the carrier protein fusion protein comprises growth hormone.

17. The method according to claim 9 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate.

18. The method according to claim 9 wherein the bone is a limb bone.

19. The method according to claim 18 wherein the limb bone is an achondroplasic bone.

20. A method for elongation of bone, comprising treating the bone in vitro with an effective amount of at least one natriuretic peptide in a pharmaceutical composition according to claim 1.

21. The method according to claim 20 further comprising inhibiting the natriuretic peptide clearance receptor.

22. The method according to claim 20 further comprising an inhibitor of the neutral endopeptidase 24.11.

23. The method according to claim 22 wherein the inhibitor of neutral endopeptidase 24.11 is thiorphan or candoxatril.

24. The method according to claim 22 wherein the step of administering an inhibitor of neutral endopeptidase is performed simultaneously with the step of administering an effective amount of at least one natriuretic peptide.

25. The method according to claim 20 further comprising an inhibitor of fibroblast growth factor receptor 3 tyrosine kinase.

26. The method according to claim 20 wherein said at least one natriuretic peptide is a natriuretic peptide fused to a carrier protein forming a natriuretic peptide-carrier protein fusion protein.

27. The method according to claim 20 wherein the carrier protein comprises growth hormone.

28. The method according to claim 20 wherein said at least one natriuretic peptide is conjugated to a carrier protein forming a natriuretic peptide-carrier protein conjugate wherein the carrier protein is selected from the group consisting of growth hormone (GH), insulin like growth factor-1 (1GF-1) and thyroid hormone (TH).

29. The method according to claim 20 wherein the bone is a limb bone.

30. The method according to claim 20 wherein the limb bone is an achondroplasic bone.

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